

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:  
MURGITROYD & COMPANY LIMITED  
Attn. Purdy, Hugh Barry  
Scotland House/165-169 Scotland Str  
GB - Glasgow G5 8 PL  
UNITED KINGDOM

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference P32890A/GTO/BPU	Date of mailing (day/month/year) 08/07/2005
International application No. PCT/GB2004/004788	FOR FURTHER ACTION      See paragraphs 1 and 4 below International filing date (day/month/year) 15/11/2004
Applicant THE QUEEN'S UNIVERSITY OF BELFAST	

1.  The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority  
European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
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Authorized officer

Stefanie Büchler

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P32890A/GTO/BPU</b>	<b>FOR FURTHER ACTION</b>	
	see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB2004/004788</b>	International filing date (day/month/year) <b>15/11/2004</b>	(Earliest) Priority Date (day/month/year) <b>14/11/2003</b>
Applicant		

THE QUEEN'S UNIVERSITY OF BELFAST

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2.  **Certain claims were found unsearchable** (See Box II).

3.  **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b.  none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB2004/004788

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - in written format
    - in computer readable form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.  
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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 12-15, 28-31, 35 and 36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-12, 14, 16 (all partially)

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12, 14, 16 (all partially)

Nucleic acids comprising the sequence shown in SEQ ID N°1 and the related subject-matter.

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2. claims: 1-12, 14, 16 (all partially)

Nucleic acids comprising the sequence shown in SEQ ID N°2 and the related subject-matter.

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3. claims: 1-12, 14, 16 (all partially)

Nucleic acids comprising the sequence shown in SEQ ID N°3 and the related subject-matter.

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4. claims: 12, 14, 16 (all partially) and 13, 15, 17, 18 (all completely)

Method of producing an antibody/hybridoma involving G-CCM cells of ECACC deposit N° 86022702 and the corresponding antibody/hybridoma from EACC deposit N° 03073001

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5. claims: 19-20 (all completely) and 23-25 (all partially)

Method of detecting an astrocytoma cell and the corresponding kit.

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6. claims: 21, 22 (all completely) and 23-25 (all partially)

Method of detecting a primary breast carcinoma cell and the corresponding kit

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7. claims: 23-25 (all partially)

Diagnostic kit for diagnosing the presence of malignant melanoma secondary tumour cells

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8. claims: 26-31

Antibodies comprising a therapeutic ligand, therapeutic antibodies and a method of treating cancer using antibodies

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9. claims: 32-36

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Anti-sense molecules and use thereof in a method of treating  
cancer

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/004788

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07K14/82	C07K14/705	C07K16/32	C12N5/12	G01N33/574
	A61K39/395	C12N15/11	A61P35/00		

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! 14 November 1997 (1997-11-14), "Homo sapiens transmembrane protein Jagged 1 (HJ1) mRNA, complete cds." XP002321955 retrieved from EBI accession no. EM_PRO:AF028593 Database accession no. AF028593 the whole document -&amp; BASH JUDY ET AL: "Rel/NF-kappaB can trigger the Notch signaling pathway by inducing the expression of Jagged1, a ligand for Notch receptors" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 18, no. 10, 17 May 1999 (1999-05-17), pages 2803-2811, XP002321954 ISSN: 0261-4189 the whole document</p>	1-12, 14, 16

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

22 March 2005

Date of mailing of the international search report

08.07.2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
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Authorized officer

Loubradou, G

## INTEFATIONAL SEARCH REPORT

National Application No  
PCT/GB2004/004788

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	<p>-&amp; LINDSELL ET AL: "Jagged a mammalian ligand that activates Notch1" CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 80, no. 6, 24 March 1995 (1995-03-24), pages 909-917, XP002090589  ISSN: 0092-8674  the whole document</p> <p>-----</p>	
X	<p>WO 98/58958 A (UNIVERSITY OF WASHINGTON; THE CHILDREN'S HOSPITAL OF PHILADELPHIA; LI,) 30 December 1998 (1998-12-30) page 22, line 28 - page 24, line 22; figure 1a</p> <p>-----</p>	1-12, 14, 16
X	<p>LI L ET AL: "THE HUMAN HOMOLOG OF RAT JAGGED1 EXPRESSED BY MARROW STROMA INHIBITS DIFFERENTIATION OF 32D CELLS THROUGH INTERACTION WITH NOTCH1" IMMUNITY, CELL PRESS, US, vol. 8, January 1998 (1998-01), pages 43-55, XP002915687  ISSN: 1074-7613  page 52, right-hand column, paragraph 3</p> <p>-----</p>	8-12, 14, 16
X	<p>GRAY G E ET AL: "HUMAN LIGANDS OF THE NOTCH RECEPTOR" AMERICAN JOURNAL OF PATHOLOGY, PHILADELPHIA, PA, US, vol. 154, no. 3, March 1999 (1999-03), pages 785-794, XP000960906  ISSN: 0002-9440  abstract  page 786, right-hand column, paragraph 2 - paragraph 3</p> <p>-----</p>	8, 12
X	<p>MULLIGAN KARL ET AL: "Expression of the MQ1 cell surface glycoprotein in human astrocytomas" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 39, March 1998 (1998-03), page 498, XP001205361  &amp; 89TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; NEW ORLEANS, LOUISIANA, USA; MARCH 28-APRIL 1, 1998  ISSN: 0197-016X  the whole document</p> <p>-----</p>	1-12, 14, 16
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national Application No  
PCT/GB2004/004788

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MULLIGAN K ET AL: "A 'new' glioma-associated cell surface glycoprotein" BRITISH JOURNAL OF CANCER, vol. 78, no. 2, July 1998 (1998-07), page 148, XP009044416 & JOINT WINTER MEETING OF THE BRITISH ASSOCIATION OF CANCER RESEARCH, THE ASSOCIATION OF CANCER PHYSIC; LONDON, ENGLAND, UK; NOVEMBER 27-28, 1997 ISSN: 0007-0920 the whole document	1-12, 14, 16
A	BOOTH CHRISTINA L ET AL: "Expression of Jagged/Notch family members in diverse tumors <i>in vivo</i> : Association <i>in vitro</i> with a transformed phenotype" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, no. 41, March 2000 (2000-03), pages 474-475, XP009044602 & 91ST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH.; SAN FRANCISCO, CALIFORNIA, USA; APRIL 01-05, 2000 ISSN: 0197-016X the whole document	
A	SUZUKI NORIAKI ET AL: "THE EXPRESSION OF NOTCH FAMILY GENES IN HUMAN PANCREATIC CANCER." DIGESTIVE DISEASE WEEK ABSTRACTS AND ITINERARY PLANNER, vol. 2003, 2003, page Abstract No. M1015, XP009044633 & DIGESTIVE DISEASE 2003; FL, ORLANDO, USA; MAY 17-22, 2003 the whole document	
A	HAQUE RAQEEB ET AL: "Demonstration of Notch-1 and Delta-like expression in human glioma cell lines and cytotoxic effect of Notch-1 inhibition." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 44, July 2003 (2003-07), page 1310, XP001205455 & 94TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; WASHINGTON, DC, USA; JULY 11-14, 2003 ISSN: 0197-016X the whole document	

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

national Application No

PCT/GB2004/004788

Patent document cited in search report	Publication date		Patent family member(s)		Publication date
WO 9858958	A 30-12-1998	US	6136952 A		24-10-2000